Results A diagnosis of COPD was significantly associated with a two- to three-fold increased risk of CV mortality compared to people without COPD. Additionally, in patients with COPD there was a significantly increased incident risk of up to almost four-fold for hypertension (rate ratio [RR]: 0.95; 95% confidence interval 0.91–0.99 to 3.57; 3.41–3.74), up to six-fold for heart failure (RR: 1.46; 1.38–1.53 to 5.94; 5.50–6.42), up to five-fold for dysrhythmia (RR: 1.19; 0.98–1.43 to 4.74; 4.27–5.26), and up to two-fold for AMI (RR: 1.18; 0.81–1.71 to 1.89; 1.71–2.09). An increased risk was also observed for stroke (hazard ratio: 1.30; 1.18–1.43) and diabetes (risk ratio: 1.25; 1.16–1.34). No data on incident risk were identified for hypercholesterolaemia. A significantly increased risk in CV mortality compared to patients without COPD was demonstrated across all severity categories of mild, moderate and severe COPD; the risk increased further with increasing severity of COPD.

Conclusions There is substantive evidence for an association between COPD and the incidence of specific cardio- and cerebrovascular acute events or diseases. To minimise the risk of poor outcomes, it is important to ensure that patients with comorbid COPD and CVD are diagnosed early and optimally managed at all levels of health-care settings.

Please refer to page A190 for declarations of interest related to this abstract.

S101 METHODS FOR ASSESSING THE SUCCESS OR FAILURE OF COPD EXACERBATION TREATMENTS IN THERAPEUTIC CLINICAL TRIALS: A META-EPIDEMIOLOGICAL SYSTEMATIC REVIEW

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Introduction The overall outcome of a COPD exacerbation (treatment success or failure) is a critical outcome for clinical trials evaluating the management of COPD exacerbations. However, trials use heterogeneous definitions and instruments to evaluate this outcome, limiting the comparability of trial results. Here, we describe how often different measurement instruments are used to evaluate the overall outcome of COPD exacerbations, aiming to promote consistency.

Methods MEDLINE and the Cochrane Airways Trial Register were systemically searched. COPD exacerbation trials (2006–2020) reporting on treatment success or failure were included. Risk of bias was assessed. The definitions and measurement instruments used to assess treatment success/failure were collected and described narratively.

Results 56/176 (31.8%) of COPD exacerbation trials assessed the overall outcome of the exacerbation (treatment success or failure). 9/56 (16.1%) of studies had a low risk of methodological bias. Two categories of outcomes evaluating treatment success or failure were identified. Twenty-four RCTs used composite endpoints consisting of several undesirable outcomes to define treatment failure. The most frequently used components were death (59%), hospital admission (52%),

Abstract S101 Table 1 Frequently used definitions of various COPD exacerbations states

Cure or Resolution	Number of Studies (n = 56)
Complete resolution of all signs and symptoms of the exacerbation.	10
Sufficient improvement of the signs and symptoms such that no additional systemic treatments were prescribed.	5
Improvement	
Improved signs and symptoms, without any new signs or symptoms.	8
Improved symptoms as evaluated by clinical scores.	6
Treatment failure	
Lack of resolution of signs and symptoms, requiring additional treatment, or death.	7
Persistence or worsening of signs and symptoms, or death.	7
Lack of resolution of signs and symptoms, or need for further treatment.	4

treatment intensification (52%) or mechanical ventilation (37%). By comparison, thirty-three RCTs used qualitative descriptions of the status of the exacerbation (such as cure, improvement or failure), which were based on the patients' symptoms and signs (table 1). The overall outcome was evaluated at different timepoints, between 2 hours and 1 year from presentation.

Conclusions There is significant heterogeneity in the instruments used to evaluate treatment success or failure in COPD exacerbation trials. Standardization could promote comparability.

S102 THE UNDER RECOGNISED ROLE OF MODERATE EOSINOPHILIA ON EXACERBATION FREQUENCY IN COPD PATIENTS: A SINGLE CENTRE STUDY

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Introduction and Objectives High eosinophil levels in patients with COPD are a well established risk factor for frequent exacerbations. Our study aimed to determine whether more moderate eosinophil levels are also a significant driver of frequent exacerbations.

Methods We retrospectively identified 213 patients who presented with a severe exacerbation of COPD to our unit from 01 January 2018 to 31 December 2018. Patients were divided into three groups: high eosinophilia (peak eosinophil level ≥ 0.5); moderate eosinophilia (peak eosinophil level 0.3–0.4) and low eosinophilia (peak eosinophil level ≤ 0.2).

The exacerbation frequency and trajectory of patients was followed up for 18 months. Standard univariate statistical analysis was undertaken to determine the impact high, moderate, and low eosinophilia had on exacerbation frequency.

Results For patients who were initially infrequent exacerbators, moderate eosinophilia was associated with a shift towards increased exacerbation frequency ($p < 0.05$). High eosinophilia however was not associated with increased exacerbation frequency ($p = 0.897$).

For patients who were initially frequent exacerbators, moderate eosinophilia was associated with a sustained high exacerbation frequency ($p < 0.05$). High eosinophilia however was not associated with a sustained high exacerbation frequency ($p = 0.2178$).

Of those patients with high eosinophilia ($n = 65$), 42.19% were on a high inhaled corticosteroid dose compared to 8.70% of those with moderate eosinophilia ($n = 70$), ($p < 0.0001$).

Conclusion Our study shows that moderately raised eosinophils in COPD are associated with significantly increased long term exacerbation frequency trends.

Our data suggests that in clinical practice high eosinophil levels in COPD patients are more readily identified by clinicians, leading to escalation in ICS therapies to successfully manage exacerbation frequencies. The significance of moderate eosinophil levels is likely under recognised and these patients may also benefit from escalation in ICS therapies.

S103 THE PROVISION OF THE FIVE FUNDAMENTALS OF COPD CARE – FINDINGS FROM A UK-WIDE SURVEY OF PEOPLE WITH COPD

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Introduction and Aims Patient-reported data on care provided for people with chronic obstructive pulmonary disease (COPD) is patchy. This research aims to understand what care is being provided to this population, and how it affects people. This data will provide the basis of recommendations for service improvements.

Methods Between December 2020 – May 2021, the Asthma UK and British Lung Foundation ran an online survey of people with COPD. The survey received 8,232 responses. Using NICE's *Five fundamentals of COPD care*,¹ respondents were asked about the care they received for their condition, as well as their experiences of living with the condition. Respondents were judged to have received the five fundamentals of care if they gave a positive answer to the elements they were eligible for (based on their MRC breathlessness score and smoking status).

Results 24.5% of all respondents received all of the measures of care they were entitled to. Considerable variation lies behind this overall figure, with rates of provision ranging from 28.5% in South West England, to 13.5% in Northern Ireland. 13.3% of respondents who told us they had more than 10 exacerbations in the past 12 months received these care measures, compared to 28.5% of people who between zero and two exacerbations in the past year. Those who have lived with COPD for over ten years were more likely (36.0% received care measures) to receive these care measures than those who have been diagnosed in the past two years (10.6%).

Conclusions This research indicates a significant proportion of people with COPD are not receiving the five fundamentals of COPD care. There is also considerable variation in provision among the COPD population, and improving care provision needs to be made a priority in order to improve clinical outcomes and reduce exacerbations.

REFERENCE

1. National Institute of Health and Care Excellence (NICE), 2018. *Chronic obstructive pulmonary disease in over 16s: non-pharmacological management and use of*

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S104 COST-EFFECTIVENESS OF TRIPLE THERAPY WITH BUDESONIDE/GLYCOPYRRONIUM/FORMOTEROL FUMARATE VERSUS DUAL THERAPIES IN MODERATE-TO-VERY SEVERE COPD IN THE UNITED KINGDOM: ANALYSIS BASED ON THE KRONOS STUDY

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Introduction The 24-week KRONOS study (NCT02497001) showed that fixed-dose triple therapy with budesonide/glycopyrronium/formoterol fumarate 320/14.4/10 µg (BGF 320) metered dose inhaler (MDI) was more efficacious at improving lung function than fixed-dose long-acting muscarinic antagonist (LAMA)/long-acting β_2 -agonist (LABA) and inhaled corticosteroid (ICS)/LABA dual therapy in symptomatic patients with moderate-to-very severe chronic obstructive pulmonary disease (COPD). In KRONOS, >70% of patients had no moderate or severe exacerbations in the previous year. Here, using KRONOS data, the lifetime cost-effectiveness of BGF 320 versus LAMA/LABA and ICS/LABA dual therapies in the United Kingdom is estimated.

Methods A Markov model was used to extrapolate incurred costs and quality-adjusted life-years (QALYs) for patients with moderate-to-very severe COPD. The model accounted for progression in severity (lung function decline), occurrence of moderate and severe exacerbations, adverse events, and discontinuations from the KRONOS study for BGF MDI 320, the LAMA/LABA glycopyrronium/formoterol fumarate 14.4/10 µg (GFF) MDI and the ICS/LABA budesonide/formoterol fumarate 400/12 µg (BUD/FORM) dry powder inhaler. Health care resource utilization was based on KRONOS data; unit costs came from UK National Health Service reference costs, the Personal Social Services Research Unit manual and the published literature. EuroQoL 5-dimension 5-level utilities for COPD severity states were estimated from KRONOS; exacerbation disutilities were sourced from a systematic literature review. A lifetime horizon was considered. Costs and QALYs were discounted at 3.5% per annum.

Results For BGF 320 versus GFF and BUD/FORM, respectively, incremental costs were £1500 and £2598, incremental QALYs were 0.49 and 0.38 and incremental exacerbation reductions were -4.29 and -1.78. The incremental cost-utility ratios (ICUR) for BGF 320 were £3082 and £6868 per QALY gained versus GFF and BUD/FORM, respectively.

Discussion Based on KRONOS data, triple therapy with BGF 320 was cost-effective versus LAMA/LABA and ICS/LABA dual therapies at the conventional UK-adopted willingness to pay (ICUR < £20000 per QALY) in a moderate-to-very severe COPD population where >70% of patients had no moderate or severe exacerbations in the prior year. The main cost-effectiveness driver for BGF 320 triple therapy versus dual therapies was the reduction in exacerbation rate, which reduced costs and preserved quality of life.

Please refer to page A190 for declarations of interest related to this abstract.